REMARKS

Claims 1-17 are all the claims pending in the application.

Claims 1-9, 11 and 13-17 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Claims 1-9, 11 and 13-17 remain rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for method of performing interactive clinical trials for testing a new drug for any known disease.

Claims 15-17 remain rejected under 35 U.S.C. 102(b) as being anticipated by Iliadis et al. (Computers and Biomedical Research (2000)) Vol. 33, pages 211-226.

The Applicants traverse the rejections and request reconsideration.

Specification/Abstract

The Applicants include a new abstract to overcome the noted objections.

Claim Rejections Under 35 U.S.C. § 112

Rejection of Claims 1-9, 11 and 13-17 based on § 112, second paragraph

Amended claims are presented. These claims are believed to be bereft of the grounds for section 112, second paragraph, rejection. Additional explanations are provided herein.

Claim 1 step (b)

Claim 1 step (b) recites:

"performing a phase I clinical research in which a clinical trial on at least a single dose is performed in parallel with performing computer simulation studies using the computer model;"

The Examiner inquires whether:

1. Is it the computer model that interacts with the simulation studies or are the two just run in paralel with no connection to one another?

2. Is simulation performed on the data from patients, for instance?

In response, the Applicants respectfully submit that:

1. The computer model does not interact with the simulation studies and they do not run in parallel either. Rather the computer model is a method for calculating some real-life variables and the simulations are the calculations of these variables on the computer.

2. By simulating the model of a disease on the computer, results about the expected real-life disease progression under drug treatment are obtained. These results of the computer simulations of the model are compared to the real-life results of disease progression, which were obtained in a real subjects undergoing drug treatment in a preclinical or clinical trials. The clinical trials are conducted in real patients (see Webster definition below) as opposed to preclinical trials that are conducted in animals.

Webster Dictionary defies clinical trial as a "A research study that tests how well new medical treatments or other interventions work in people. Each study is designed to test new methods of screening, prevention, diagnosis, or treatment of a disease."

In order to compute the disease progression, the computer simulations of the model need some input values, such as: i) the initial status of the patient's disease; ii) weight; iii) blood counts of the patient, etc.

Claim 1 step(b) has been amended to recite "simulations of the computer model" instead of "simulation studies using the computer model".

Claim 1 step (c).

Claim 1 step (c) recites "adjusting the computer model based on comparison of the results of the clinical research and the computer simulation;"

The Examiner contends that:

1. No "real life clinical trial" is claimed such that the comparison step in the claim is clear.

2. No equations are clear such that it is clear that the model can be adjusted.

In response, the Applicants respectfully submit:

1. In order to claim real life clinical step c has been amended to recite: "clinical trial" instead of "clinical research". Moreover, the term "clinical trial" as used by someone

skilled in the art always refers to a real life clinical trial as it is conducted in people (see Webster definition above).

2. A computer model is claimed. The computer model is a mathematical model of a disease or of biological processes related to the disease, which is written in a computer language. The mathematical model consists of equations. An example of such a model constituting of equations can be found in our US patents 6,871,171 and 7,133,814 titled "System and methods for optimized drug delivery and progression of diseased and normal cells" and European patent EP 1485818 ([146]-[173])

Claim 2

Claim 2 recites:

"The method of claim 1, wherein in step b, prior to each sub-step of the phase I trial, computer simulation is performed to predict results of the sub-step and the predicted results are compared to clinical results corresponding to the sub-step and the computer model is adjusted based on the comparison."

1. Examiner asked for clarification "as to what about the comparison is used to adjust the computer model". The Examiner alleges that the explanation given in reply to the previous office action is not persuasive, as no "real life clinical study" is claimed such that the comparison in claim is clear.

2. No equations are claimed such that it is clear that the model can be adjusted.

The Applicants respectfully submit that:

1. A person skilled in the art would often interchange between the term clinical trial and term clinical study. For consistency, all claims have been amended to recite "clinical trial" rather than "clinical study" or "trial". The Applicants further clarify that the user compares the results of each sub-step of phase I clinical trial to the results of the computer simulations of the model (predictions) performed prior to each sub-step of phase I clinical trial. In case these predictions turn out to be less accurate than required, the model should be changed/ adjusted so that simulating the adjusted model gives more accurate results (predictions). The model is adjusted by changing the equations to yield different outcomes which will be more similar to the outcomes of the clinical trial conducted in real life.

Rejection of Claims 1-9, 11 and 13-17 based on § 112, first paragraph

For a speedier prosecution of the case, the independent claims are amended to indicate cancer related studies for a drug. The Applicants reserve the right to file continuing Applications devoted to claims having a broader scope of coverage.

Claims Rejections Under 35 U.S.C. § 102

Rejection of Claims 15-17 based on Iliadis et al.

The Examiner contends that Iliadis et al. teaches a method in which optimization of cancer treatment is determined by using a mathematical model describing pharmacokinetics of anticancer drugs, antitumor efficacy, and drug toxicity.

However, Iliadis et al. merely suggest a method for finding optimal drug regimens. In no way are they trying to implement this method in the process of clinical trials conducted for a drug under development, which is the subject matter of the current application. Specifically,

Iliadis et al. conducted no trial. For the conventional treatment regimen they used literature data. They didn't conduct a trial to check/validate whether the simulations results of their suggested optimal regimen are indeed feasible and superior to conventional regimen therapy.

Iliadis does not suggest applying their method to a new drug under development. Rather, to verify their model they used clinical results of the drug etoposide, which was a drug on market (first approved on Dec 30 1986; see approval summary in the FDA site http://www.accessdata.fda.gov/scripts/cder/onctools/summary.cfm?ID=92).

A short summary of the Iliadis et al paper:

1. First describe the mathematical model (p.212-216) and a method for using the model to obtain optimal drug regimens (p.216-217).

2. The model is, then, tested/validated to assure that the method for obtaining the optimal drug regimen using the model is indeed accurate in the simulation study section (p.217-222). This is done by taking 5 conventional clinical protocols (regimens) proposed for cancer treatment (p 218 paragraph 5) of the drug on market, etoposide (p. 217 paragraph 4). It is important to note that by "clinically used protocols" the authors mean protocols that were approved by FDA and used as a conventional treatment in the clinic by the doctor.

3. These 5 protocols are simulated by the model "First, we simulated the fate of the drug concentrations, tumor size, and WBC count through the conventional clinical protocols.." (p. 218 paragraph 5) as indicated by the examiner. The simulation results are depicted in Figure 2 p. 220.

4. The simulation results are compared to the available data on the literature about the results of these treatments to confirm the accuracy of the model: "These findings on tumor fate as well as on the simulated plasmatic concentrations and WBC count characteristics are

consistent with the data in the literature. (p. 219 paragraph -2) and "data related to etoposide investigations were used in a feasibility study" (abstract).

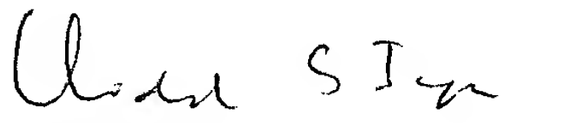
5. The confirmed model is used to suggest optimal drug regimen. Finally, the paper showed that the simulation results of the proposed regimen are superior to those of conventional regimen: "Simulations with the optimized protocol showed better performances than usual clinical protocol." (abstract)

The Examiner has not established *prima facie* obviousness of claims 15-17 based on Iliadis because of the above-noted differences between the present invention and Iliadis.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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